REMARKS

Initially, Applicants note that the Examiner has still failed to acknowledge Applicants' claim to priority and receipt of the certified copy of the priority document.

Hence, once again, the Examiner is kindly requested to acknowledge Applicants' claim to priority and receipt of the certified copy of the priority document which was filed on January 24, 2000.

In paragraph 1, on page 2 of the Office Action, the Examiner objects to the Abstract because it is less than 50 words.

Applicants respectfully that the Examiner's rejection is improper. The rule, i.e., 37 C.F.R. § 1.72(b), states that the Abstract may not exceed 150 words in length. There is no minimum number of words for the Abstract. The Examiner's citation of the MPEP to support her position that the Abstract should be limited to a single paragraph in the range of 50 to 150 words is merely a general guideline and not the rule. The rule sets forth the maximum number of words, not the minimum number of words. The present Abstract is about 26 words, and thus clearly is appropriate.

Claim 43 has been amended to delete the expression "so as to inhibit the localization of PKA type Iα isozyme with T cell receptor/CD3 complexes". The original claims referred to "anchoring disruptive peptides" which would have had this effect. However, the antagonists now recited in Claim 43 do not function in this way (see page 5 of the present application). Reference to

"antagonist" in Claim 43 is believed to adequately define the mode of action of the claimed compounds.

In paragraph 4, on page 3 of the Office Action, the Examiner rejects Claims 45-50 under 35 U.S.C. § 112, second paragraph.

Specifically, the Examiner states that Claim 45 is indefinite in that it fails to recite a final step that relates back to the preamble, i.e., a method of treatment of an immunosuppressive disease.

For the following reasons, Applicants respectfully traverse the Examiner's rejection.

There is only one step to the claimed invention, i.e., administration of the pharmaceutical composition containing the active ingredient, i.e., the cAMP antagonist. Thus, there is no need to include a "final step" as contended by the Examiner. However, in order to advance prosecution, Applicants hereby amend paragraph (A) of Claim 45 to set forth that the pharmaceutically effective amount is an amount effective to treat an immunosuppressive disease selected from the group consisting of those recited in Claim 50, which is hereby cancelled.

Accordingly, Applicants respectfully submit that the claims clearly and definitely recite the invention of interest, and thus request withdrawal of the Examiner's rejection.

In paragraph 6, on page 3 of the Office Action, the Examiner rejects Claims 40-50 under 35 U.S.C. § 112, first paragraph.

Specifically, the Examiner states that while the specification is enabling for the treatment of CVI, AIDS or HIV infection by administering Rp-8-Br-cAMPS, Rp-8-Cl-cAMPS and Rp-8-Br-monobutyryl-cAMPS, such does not provide enablement for any cAMP antagonist.

For the following reasons, Applicants respectfully traverse the Examiner's rejection.

Applicants respectfully submit that the Examiner's rejection is improper with respect to Claims 40-42, since these claims are composition claims, and it only necessary to provide enablement for one utility of a composition claim. The Examiner has admitted that the specification in enabling for treatment of three diseases, i.e., CVI, AIDS or HIV, and thus no more needed with respect to these composition claims.

Furthermore, Applicants respectfully submit that the Examiner's rejection is improper with respect to Claims 43-44, since these claims are not directed to a method of treatment, but rather to a method of inhibiting the effects of PKA type-I isoenzyme.

The Examiner is requested to note that Claims 40 and 43, are limited to 5 specific cAMPS antagonists, 2 of which the Examiner admits are enabling, and Claim 45 covers a 3rd cAMPS antagonist which the Examiner admits is enabling. Applicants respectfully submit that is not legally necessary to provide evidence with respect to every single antagonist claimed, but merely a representative number of examples thereof. As evidence as to 2 out of 5 of the specified antagonists, plus a 3rd, has been provided, Applicants respectfully submit that evidence with

respect to a representative number has been shown with respect to the claims.

As to Claims 45-50, as noted above, Applicants hereby amend Claim 45 to include the recitation of Claim 50 therein, which is hereby cancelled. That is, Applicants hereby amend Claim 45 to recite treatment of the three diseases, i.e., CVI, AIDS or HIV, which the Examiner has admitted are enabled by the specification.

In the Amendment filed June 19, 2002, Applicants provided convincing data for a cAMP antagonist which the Examiner has accepted as showing an increase in T-cell immune function *in vivo*. Applicants also submitted data showing that two further cAMP antagonists which are structurally related to Rp-8-Br-cAMPS, and would be expected to function in the same way, show effects *in vitro* indicating that there is good reason to believe that they would, in fact, function similarly *in vivo*.

In view of this, Applicants clearly identified a target in PKA type Iα that serves as a key negative regulator of lymphocyte function. Prior to the Applicants' invention, the role of cAMP levels in T-cells in cell proliferation and immune responses in physiological conditions was not known. In addition, the role of specific PKA isoenzymes in T-cell functioning had not been fully elucidated. Applicants have identified and utilized PKA isozyme specific cAMP antagonists and have successfully shown that they are useful in treating immunosuppressive diseases. The contribution to the art is therefore the identification of a specific isozyme target. Antagonists of this target have been shown to have the desired

effects both *in vitro* and *in vivo*. This demonstrates that interference at the level of the PKA type Iα isozyme is effective in treating immunosuppressive diseases.

It is entirely appropriate (and commensurate with the contribution made to the art) to claim a wider range of cAMP antagonists than those that have specifically been shown to function *in vivo*. Once it is known that the target is useful, the type and nature of the cAMP antagonists used may be modulated and varied as it would be expected that any compound that interferes with the PKA type Iα isozyme will have this effect both *in vitro* and *in vivo*. The data in the application and submitted in the Declaration filed June 19, 2002, supports this assertion. It is entirely within the skilled persons' competence to identify such useful molecules by testing their antagonistic function against the specific isozyme.

In any event, Applicants amend Claim 45 to include the recitation of Claim 46 therein, which is hereby cancelled. That is, Applicants amend Claim 45 to recite the relevant target, i.e., said cAMP antagonist selectively or specifically abolishes the function of cAMP dependent protein kinase (PKA) type Iα isozyme ($RI\alpha_2C_2$).

Once the relevant target has been identified, as it has, any compound that would be able to target that isozyme would have the desired effect *in vivo*. This is supported in the application by the fact that a number of different types of inhibitors, such as ribozymes or antisense nucleic acids or peptides, that inhibit the localization of PKA also had the desired effect *in vitro*. This amendment effectively introduces

a functional requirement into Claim 45, i.e., only antagonists to the specified molecule are encompassed thereby, and thus only those molecules which work according to the invention are claimed.

Accordingly, Applicants respectfully submit that the claims are enabled by the present specification, and thus request withdrawal of the Examiner's rejection.

In paragraph 8, on page 7 of the Office Action, the Examiner rejects Claims 40-42 under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent 5,842,916 (Chuo-Chung et al).

Specifically, the Examiner states that Chuo-Chung et al teaches pharmaceutical compositions comprising Rp-8-cAMPS and Rp-8-Cl-cAMPS.

For the following reasons, Applicants respectfully traverse the Examiner's rejection.

Contrary to the Examiner's contention, Claims 40-42 do not cover Rp-8-Cl-cAMPS. Further, Chuo-Chung et al does not teach Rp-8-Br-cAMPS as recited in Claims 40-42, but rather Chuo-Chung et al merely teaches Sp-8-Br-cAMPS.

Accordingly, Applicants respectfully submit that the present invention is not taught or suggested in Chuo-Chung et al, and thus request withdrawal of the Examiner's rejection.

In view of the amendments to the claims and the arguments set forth above, reexamination, reconsideration and allowance are respectfully requested.

The Examiner is invited to contact the undersigned at his Washington telephone number on any questions which might arise.

Respectfully submitted,

Gordon Kit
Registration No. 30,764

SUGHRUE MION, PLLC
Telephone: (202) 293-7060
Facsimile: (202) 293-7860

Date: January 10, 2003

A P P E N D I X

IN THE CLAIMS:

The claims are being amended as follows:

Claim 43. (Amended) A method of inhibiting the effects mediated by PKA type Iα isozyme comprising administering to subject in need of said inhibition, a pharmaceutical composition comprising:

(A) a pharmaceutically effective amount of a cAMP antagonist, wherein said cAMP antagonist is selected from the group consisting of Rp-8-Br-cAMPS, Rp-8-Br-monobutyryl-cAMPS, Rp-monobutyryl-cAMPS, Rp-8-(4-chlorophenyl-thio)-cAMPS and Rp-piperidino-cAMPS; and

(B) a pharmaceutically acceptable adjuvant or filler[, so as to inhibit the localization of PKA type Iα isozyme with T cell receptor/CD3 complexes].

Claim 45. (Amended) A method of treating a subject afflicted with an immunosuppressive disease, comprising administering to said subject a pharmaceutical composition comprising:

(A) a pharmaceutically effective amount of a cAMP antagonist sufficient to treat an immunosuppressive disease selected from the group consisting of AIDS, HIV infection and CVI, wherein said cAMP antagonist selectively or specifically abolishes the function of cAMP dependent protein kinase (PKA) type Iα isozyme ($RI\alpha_2C_2$); and

(B) a pharmaceutically acceptable adjuvant or filler.

Claim 47. (Amended) The method of Claim [46] 45, wherein said cAMP antagonist is a thio-substituted cAMP analog, wherein

said thio-substituted cAMP analog is an equatorial diastereomer of 3',5'-cyclic adenosine monophosphorothioate (Rp-cAMPS), and wherein said thio-substituted cAMP analog binds to an RIα subunit of said isozyme and acts as a selective or specific antagonist of said isozyme.

Claims 46 and 50 are being cancelled.